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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/042,711 | 12/12/2001 | Jennifer June Brown | ENZ-57 (CIP) (C) | 4374 |

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ENZO BIOCHEM, INC.
527 MADISON AVENUE (9TH FLOOR)
NEW YORK, NY 10022

| EXAMINER | |
|---|---|
| FALK, ANNE MARIE | |
| ART UNIT | PAPER NUMBER |
| 1632 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/042,711 | BROWN ET AL. | |
| | Examiner | Art Unit | |
| | Anne-Marie Falk, Ph.D. | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *39,43,49-51,58,60,62,63,69 and 71-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39,43,49-51,58,60,62,63,69 and 71-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 December 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The amendment filed March 25, 2009 has been entered. Claims 39, 49, 51, 58, 60, and 69 have been amended. Claims 34-38, 41, 42, 44-48, 52-57, 61, and 64-68 have been cancelled.

Accordingly, Claims 39, 43, 49-51, 58, 60, 62, 63, 69, and 71-74 remain pending in the instant application.

The remarks filed December 23, 2008 (hereinafter referred to as "the response") are considered herein.

The elected invention is drawn to a method for developing a therapeutic procedure in a model animal system (*in vivo* testing of a procedure).

Claims 39, 43, 49-51, 58, 60, 62, 63, 69, and 71-74 are examined herein.

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 25, 2009 has been entered.

The rejection of Claims 51, 58, and 60-63 under 35 U.S.C. 112, second paragraph, is **withdrawn** in view of the amendments to these claims.

The rejection of Claims 69 and 73 under 35 U.S.C. 102(b), as being anticipated by Yan et al. (1996), is withdrawn in view of the amendment to Claim 69.

***Priority***

Applicant's claim for domestic priority under 35 U.S.C. § 120 is acknowledged. However, the non-provisional applications upon which priority is claimed fail to provide adequate support under 35 U.S.C. 112 for Claims 39, 43, 49-51, 58, 60, 62, 63, 69, and 71-74 of this application. The earlier-filed application does not disclose an animal model as recited in the instantly claimed methods.

Applicants did not address this issue in the most recent response.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***Enablement***

Claims 39, 43, 49-51, 58, 60, 62, 63, 69, and 71-74 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of *Tupaia belangeri* infected with HIV-1 or HBV in the claimed method for developing a therapeutic procedure, does not reasonably provide enablement for the use of any *Tupaia* species or for other human pathogens. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method for developing a therapeutic procedure, wherein the method involves the use of any *Tupaia* species as recited in the claims. Claims 58, 63, 69, and 74 are directed to infecting a *Tupaia* with any human viral pathogen. Claim 71 is directed to infecting a *Tupaia* with any human retrovirus.

The specification fails to provide an enabling disclosure for the use of any *Tupaia* species as an animal model for any human viral pathogen. The claims encompass the use of any *Tupaia* species as a

model for infection with any human viral pathogen. However, the specification only discloses *Tupaia belangeri* as an animal model for HBV and HIV-1 infections. No guidance is offered with regard to how one skilled in the art would develop other *Tupaia* species as animal models for human viral pathogens. No other human viral pathogens were examined for their capacity to infect any other *Tupaia* species. No other *Tupaia* species were examined for their susceptibility to any other human viral pathogen. There are numerous human viral pathogens including retroviruses, lentiviruses, parvoviruses, paramyxoviruses, orthomyxoviruses (influenza), hepadnaviruses, herpesviruses, papillomaviruses, rhabdoviruses, and poxviruses, to name just a few. The claims cover the use of any *Tupaia* species infected with any human viral pathogen. No guidance is offered with regard to the numerous parameters that must be examined to determine if one or more of the other *Tupaia* species are susceptible to infection by any single human viral pathogen. Furthermore, genetic modification may be used to render a *Tupaia* animal susceptible to infection by a human viral pathogen. The claims encompass genetically modified animals, but the specification does not disclose any genetic modifications that could be made to render a given animal susceptible to infection by a given human viral pathogen. The instant specification only deals with two viral pathogens and their infectivity in a single species of animal. Animal models of human infectious disease are notoriously unpredictable as evidenced by the numerous attempts to produce or identify a suitable animal model for HIV infection (see Lewis et al., 1995). Lewis et al. (1995) discuss the many problems that exist with regard to the disease characteristics displayed by the best animal models for HIV infection. None of the animal models exhibit the ideal characteristics as outlined in Box 1, page 144. Thus, despite an enormous amount of data on the HIV virus and its role in causing AIDS, and despite intense efforts to generate an adequate animal model, significant deficiencies remain.

Given the lack of specific guidance in the specification with regard to generating or identifying *Tupaia* animal models for human viral pathogens, the limited working examples disclosed, and the unpredictability in the art for developing animal models of human infectious diseases, one skilled in the

art would have been required to engage in undue experimentation to produce the claimed *Tupaia* animal models over the full scope and to use the animal models in the claimed methods.

At page 8 of the response, Applicants allege that the claims are fully enabled and that, solely in an effort to promote prosecution, Claims 39 and 49 have been amended to recite that the human viral pathogen is HIV-1 or HIV-2. First, both Claims 39 and 49 continue to recite that the human viral pathogen may be HCV, in addition to HIV-1 or HIV-2. Second, all pending claims, including Claims 39 and 49, remain broader than the indicated scope of enablement and Applicants have not provided adequate arguments or evidence with regard to this broader scope.

At page 9 of the response, Applicants take issue with the statement "[t]he claims encompass the use of any *Tupaia* species as an animal model for infection with any human viral pathogen." Applicants point to the specification for noting three separate viral pathogens (HBV, HCV, and HIV) as being almost exclusively infective in humans. Applicants argue that the fact that these pathogens are infectious in *Tupaia belangeri* argues for a remarkable conservatism in *Tupaia* that extends from when there was a common ancestor shared by humans and *Tupaia*. However, the fact that chimpanzees are not susceptible to this scope of human viral pathogens, argues against conservation across *Tupaia* species.

At page 9 of the response, with regard to the parameters that would be examined to determine if a *Tupaia* species was susceptible to a human viral pathogen, Applicants allege that the symptoms and effects would be well known for any given human viral pathogen and it would be an obvious approach to investigate the well-known parameters associated with the disease caused by that virus. However, there is no evidence that any given species of *Tupaia* would be suitable as an animal model for any given human virus, other than those set forth above. In particular, there is no evidence that the symptoms observed in humans would also be observed in the various *Tupaia* species covered by the claims, for any given human virus, and the evidence of record shows that animal models of human infectious disease are notoriously unpredictable. Given the very broad scope of the claims, which includes genetic manipulations to

enhance viral susceptibility, and the very limited guidance in the specification, the skilled artisan would have been required to engage in undue experimentation to practice the claimed methods over the full scope.

***Written Description***

Claims 39, 43, 49-51, 58, 60, 62, 63, 69, and 71-74 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to the use of a *Tupaia* species as an animal model for infection with a human viral pathogen and methods for developing a therapeutic procedure.

The claims encompass the use of any *Tupaia* species as a model for any human viral pathogen in the claimed methods. However, the specification only discloses two animal model systems. *Tupaia belangeri* were shown to be susceptible to infection by HBV and HIV-1. No other human viral pathogens were examined for their capacity to infect any *Tupaia* species. No other *Tupaia* species were examined for their susceptibility to any human viral pathogen. There are numerous human pathogens including retroviruses, lentiviruses, parvoviruses, paramyxoviruses, orthomyxoviruses (influenza), hepadnaviruses, herpesviruses, papillomaviruses, rhabdoviruses, and poxviruses, to name just a few. The claims cover the use of any *Tupaia* species. Furthermore, genetic modification may be used to render a *Tupaia* animal susceptible to infection by a human viral pathogen. The claims encompass genetically modified *Tupaia* animals, but the specification does not disclose any genetic modifications that could be made to render a *Tupaia* animal susceptible to infection by a human viral pathogen. The instant specification only deals with two viral pathogens and their infectivity in a single species of *Tupaia*. Thus, the specification does

not disclose a representative number of model systems that include a representative number of *Tupaia* species in combination with a representative number of human viral pathogens. In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In this case, only two animal models are disclosed. Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. In this case, no other relevant identifying characteristics have been disclosed. The specification does not teach a generally applicable methodology that can be used to identify animal species that can be productively infected with a given human viral pathogen. This limited information regarding the claimed embodiments is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of the full scope of *Tupaia* animal models at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

With regard to the claimed methods for developing a therapeutic procedure, adequate written description is not provided. The specification does not disclose any process developed or derived from any animal model as set forth in the claims. Even as relates to the disclosed *Tupaia* animal models, no screening methods are disclosed as such. The absence of any written description of screening methods as claimed does not satisfy the written description requirement for the claimed genus. Thus it is concluded that the written description requirement is not satisfied for the claimed methods.

At pages 11-12 of the response, Applicants assert that the claims relate only to HCV, HIV-1, and HIV-2, as the particular human viral pathogens. This is not correct, as the claims continue to be broadly drawn to the use of any human viral pathogen. Claims 58, 63, 69, and 74 remain directed to the use of **any** human viral pathogen. With regard to HCV, Applicants assert that it was known in 1998 that HCV could infect *Tupaia* at least transiently, citing Xie et al. (1998) Virology 244: 513-520. The Examiner cannot comment on evidence that is not of record. The Xie et al. reference was not provided with

Applicants' response and is not cited on the IDS. At page 11, paragraph 1 of the response, Applicant's continue their argument premised on the reference of Xie et al., and further cite Zhao et al. (2000) and Xu et al. (2007) for demonstrating certain properties of the HCV virus or its infection. The evidence presented is not commensurate in scope with the scope of the claims, which is directed to the use of any *Tupaia* species infected with any human viral pathogen (see especially Claims 58, 63, 69, and 74).

At page 12 of the response, Applicants assert that, with regard to retroviruses a number of these viruses are known to have extremely wide host ranges such that they are infective towards humans as well as mice, and that viruses grown in mouse cells may be later used for infection of human subjects. It is unclear what Applicants are attempting to argue or how this relates to the claims which are directed to the use of various *Tupaia* species. Furthermore, Applicants are reminded that Attorney argument cannot take the place of actual evidence. No evidence pertaining to viruses grown in mouse cells has been provided. See MPEP § 2145 and 716.01(c)(II). The arguments of counsel cannot take the place of evidence in the record. *In re Schulze* 145 USPQ 716, 718 (CCPA 1965).

At page 13 of the response, Applicants assert that HIV was shown in the specification as capable of infecting *Tupaia* thereby showing that a number of retroviruses should be infective towards this lower primate animal model. However, given the evidence of record, there is no basis for concluding that one retrovirus is representative of all retroviruses. There is no evidence that HIV is representative of all other retroviruses, or that other retroviruses would have the same host range as the exemplified HIV. The evidence of record shows that animal models of human infectious disease are notoriously unpredictable (see Lewis et al., 1995). Numerous attempts to produce or identify a suitable animal model for HIV infection have met with limited success (Lewis et al., 1995). The prior art shows that macaques, baboons, chimpanzees, pig-tailed macaques, and gibbons are susceptible to infection with HIV. Thus, the nonhuman host range is extremely limited. Further, the pathogenesis varies substantially from species to species. Lewis et al. (1995) discuss the many problems that exist with regard to the disease

characteristics displayed by the best animal models for HIV infection. Furthermore, animal models require extensive characterization before they can be used in pre-clinical testing (see Lewis et al., page 149, column 1, paragraph 1). Intensive effort has been applied to developing animal models of HIV and other viral diseases with limited success.

At pages 12-13 of the response, Applicants assert that animal models of human diseases can be used to understand the progression and nature of a disease caused by a pathogen. Applicants further assert that they can be used to serve as surrogates for the development of therapeutic procedures. Applicants allege that the methods used for both of these uses are well known in the art, and a user would understand procedures that could and would be used after disclosure of the novel animal models of the present invention. Applicants go on to note that Example 2 is a demonstration of oral tolerance in Tupaia to HBV, which resulted in an alleviation of liver destruction by autoimmune responses. As regards Example 2, the Examiner has already acknowledged an enabled scope for methods that include infection of *Tupaia belangeri* with HBV. Thus, this is not part of the rejected scope. As regards the alleged well known procedures for the development of therapeutic procedures, while the skilled artisan would know the disease symptoms displayed by humans for any given human viral pathogen, the artisan would not know the disease symptoms displayed by any given *Tupaia* species to the multitude of human viral pathogens encompassed by the claims. As the art of record shows, different animals exhibit different symptoms and most do not exhibit the same symptoms seen in humans. As Lewis et al. shows, animal models require extensive characterization before they can be used in pre-clinical testing and the instant specification provides **no** information with regard to *Tupaia* species other than *Tupaia belangeri* or for human viral pathogens other than HIV-1 and HBV. Given the unpredictability in the art, for reasons of record, the specification provides no guidance as to what symptoms would be exhibited by *Tupaia* species, other than *Tupaia belangeri* infected with HIV-1 or HBV, for a given human viral pathogen, such as influenza virus, HPV, measles, or mumps virus.

***Conclusion***

No claims are allowable.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

/Anne-Marie Falk/
Primary Examiner, Art Unit 1632